

SEQUENCES OF PROTEINS OF IMMUNOLOGICAL INTEREST

FIFTH EDITION

Kabat

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In Fig. 1 and in the stereomodels of antibody combining sites, the location of the allotypic regions may clearly be seen to be on the outside of V_h away from the combining site. Residues 9 and 65 of V_h are numbered and will facilitate location of the V_h a allotypes. The few cDNA sequences available in 1984 (65) provided no evidence that germ line sequences encoding latent allotypes may exist in some rabbits. Since then, additional germline and expressed V_h a sequences (63-65, 188, 204-206) have further refined the information on V_h a allotypes and V_h a⁻ sequences. Newer analyses of germline V_h genes of rabbits have provided examples of potential genes and pseudogenes which could generate latent allotype sequences by somatic gene conversion mechanisms (187, 199, 203-208). Antisera to rabbit V_h a allotypes crossreact with human IgG, various other species of IgM and IgG, and with the Galapagos shark 7S immunoglobulin and correlate with the N-terminal amino acid sequence (209, 210).

It is becoming of great importance, with all of the different mechanisms which are clearly generating diversity, to evaluate the extent to which each type of diversity, other than those resulting in pseudogenes, contributes noise rather than functional differences in complementarity of antibody combining sites (70, 211).

Ohno et al. (212, 213) have proposed that the genes coding for variable domains of the light and heavy chains arose from tandem repeats of a primordial nucleotide sequence about 48 base pairs in length which subsequently diverged by mutations and deletions producing a resemblance to FR1, FR2, and FR3. The complementary strand of the primordial 48 base pair repeat of V_L became the primordial V_h . The finding (147) that the complementary strands of the human D2 and D4 minigenes coded for a portion of CDR1 of V_h tends to support this hypothesis. A 45 base pair primordial building block has also been proposed for the gene for the class I major histocompatibility complex (214).

The format of our precursor, V-region, C region sequences etc. of antibodies and T cell receptors has proven very useful in selecting primers for the polymerase chain reaction (215-217).

Constant Region Sequences

The constant region sequences were aligned in such a manner as to permit various comparisons of the light chain (C_L) and the individual domains of the heavy chain (C_h 1, C_h 2, C_h 3, and C_h 4). This was accomplished by sequential numbering on the left with gaps inserted for alignment. The following numbering system is used:

108 to 215 of C_L ;
 114 to 223 of C_h 1, plus the first part of hinge (224 to 241),
 the end of hinge (242 and 243), and the
 first two residues of CH2 (244 and 245);
 246 to 360 of C_h 2;
 361 to 496 of C_h 3;
 497 to 628 of C_h 4.

The gene quadruplication in the human IgG3 hinge region (218) is numbered differently using letters 241A to 241Z, and 241AA to 241SS, and these residues should not be used in aligning domains for homology. The next two columns in the heavy chain tables indicate the EU (67) and OU (219) residue numbers, respectively. The succeeding columns which are numbered give the sequence data. The C_h and hinge domains conform to the findings of Sakano et al. (220), who defined each domain precisely by sequencing the coding and intervening nucleotide sequences bordering each domain.

The extensive nucleotide sequence data on exons for the constant regions of heavy chains have provided exact boundaries for C_h 1, hinge, C_h 2, C_h 3, and C_h 4. Usually the introns separating these domains fall within the codon for a single amino acid. We have included that amino acid residue with the domain, the exon of which contains two of the three coding nucleotides. The constant regions

HEAVY CONSTANT CHAINS CB2 REGION

HEAVY CONSTANT CHAINS CB2 REGION (cont'd)

HEAVY CONSTANT CHAINS CH₂ REGION (cont'd)

HEAVY CONSENSE CHAINS CB2 REGION (cont'd)

HEAVY CONSTANT CHAINS CH₂ REGION (cont'd)

EU INDEX	OU INDEX	81	82	83	84	85	86	87	88	89	90	91	92	93	94	95	96	97	98	99
		IGG1 % CL	IGG1 % CL	MOPC 21	IF2 %	ICR 11.19.3	IGG2B %	IGG2B %	IGG2B %	IGG2B %	MPC %	10.1	IGG2A %	IGG2A %	IGG2A %	IGG2A %	MOPC 101	CBP %	IGA %	
243A		---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	
243B		---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	
243C		230	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	
243D		231	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	
243E		232	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	
244	231	VAL	VAL	VAL	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	
245	232	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	
245A		---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	
245B		---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	
245C		---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	
246	233	233	---	---	---	---	ASN	ASN	ASN	ASN	ASN	ASN	ASN	ASN	ASP	ASP	ASP	ASP	ASP	
247	234	234	---	---	---	---	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	
248	235	235	---	---	---	---	GLU	GLU	GLU	GLU	GLU	GLU	GLU	GLU	GLU	GLU	GLU	GLU	GLU	
249	236	236	GLU	GLU	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	
250	237	237	VAL	VAL	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	
251	238	238	SER	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	
251A		---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	
251B		---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	
252	239	239	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	
253	240	240	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	
254	241	241	PHE	PHE	PHE	PHE	PHE	PHE	PHE	PHE	PHE	PHE	PHE	PHE	PHE	PHE	PHE	PHE	PHE	
255	242	242	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	
256	243	243	PHE	PHE	PHE	PHE	PHE	PHE	PHE	PHE	PHE	PHE	PHE	PHE	PHE	PHE	PHE	PHE	PHE	
257	244	244	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	
258	245	245	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	
259	246	245	LYS	ASN	ASN	ASN	ASN	ASN	ASN	ASN	ASN	ASN	ASN	ASN	LYS	LYS	LYS	LYS	LYS	
260	247	246	PRO	PRO	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	
261	248	247	LYS	LYS	LYS	LYS	LYS	LYS	LYS	LYS	LYS	LYS	LYS	LYS	LYS	LYS	LYS	LYS	LYS	
262	249	248	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	
263	250	250	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	
264	251	249	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	
265	252	250	THR	THR	MET	MET	MET	MET	MET	MET	MET	MET	MET	MET	MET	MET	MET	MET	MET	
266	253	251	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	
267	254	252	THR	THR	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	
268	255	253	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	LEU	
269	256	254	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	
270	257	255	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	
271	258	256	LYS	LYS	LYS	LYS	LYS	LYS	LYS	LYS	LYS	LYS	LYS	LYS	LYS	LYS	LYS	LYS	LYS	
272	259	257	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	
273	260	258	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	THR	
274	261	259	CYS	CYS	CYS	CYS	CYS	CYS	CYS	CYS	CYS	CYS	CYS	CYS	CYS	CYS	CYS	CYS	CYS	
275	262	260	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	
276	263	261	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	
277	264	262	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	
278	265	263	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	
279	266	264	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	
280	267	265	SER	SER	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	
281	268	266	LYS	LYS	GLU	GLU	GLU	GLU	GLU	GLU	GLU	GLU	GLU	GLU	GLU	GLU	GLU	GLU	GLU	
282	269	267	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	
283	270	268	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	
284	271	269	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	PRO	
285	272	269	GLU	GLU	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	
286	273	269	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	GLN	
287	274	269	PHE	PHE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	ILE	
288	275	269	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	
289	276	270	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	SER	
290	277	271	TRP	TRP	TRP	TRP	TRP	TRP	TRP	TRP	TRP	TRP	TRP	TRP	TRP	TRP	TRP	TRP	TRP	
291	278	272	PHE	PHE	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	
292	279	273	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	
293	274	274	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	
294	275	275	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	
295	280	276	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	
296	281	277	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	ASP	
297	282	278	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	
298	283	279	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	
299	282	280	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	
300	283	281	GLU	GLU	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	VAL	
301	284	282	HIS	HIS	HIS	HIS	HIS	HIS	HIS	HIS	HIS	HIS	HIS	HIS	HIS	HIS	HIS	HIS	HIS	
302	285	283	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	
303	286	284	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	
304	287	285	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	
305	288	286	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	
306	289	287	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	
307	290	287	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	
308	291	289	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	
309	292	290	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	
310	293	291	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	
311	294	292	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	
312	295	293	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	
313	296	294	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	ALA	
314	315	314	ASN	ASN	ASN	ASN	ASN	ASN	ASN	ASN	ASN	ASN	ASN	ASN	ASN	ASN	ASN	ASN	ASN	
315	316	315	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	GLY	
316	317	316	LYS	LYS	LYS	LYS	LYS	LYS	LYS	LYS	LYS	LYS	LYS	LYS	LYS	LYS	LYS	LYS	LYS	
317	318	317	GLU	GLU	GLU	GLU	GLU	GLU	GLU	GLU	GLU	GLU	GLU	GLU	GLU	GLU	GLU	GLU	GLU	
318	319	318	PHE	PHE	PHE	PHE	PHE	PHE	PHE	PHE	PHE	PHE	PHE	PHE	PHE	PHE	PHE	PHE	PHE	
319	320	319	LYS	LYS	LYS	LYS	LYS	LYS	LYS	LYS	LYS	LYS	LYS	LYS	LYS	LYS	LYS	LYS	LYS	
320	321	320	CYS	CYS	CYS	CYS	CYS	CYS	CYS	CYS	CYS	CYS	CYS	CYS	CYS	CYS	CYS	CYS	CYS	
321	322	321	ARG	ARG	ARG	ARG	ARG	ARG	ARG	ARG	ARG	ARG	ARG	ARG	ARG	ARG	ARG	ARG	ARG	
322	323	322	ALA	ALA</																

HEAVY CONSTANT CHAINS CH₂ REGION (cont'd)

HEAVY CONSTANT CHAINS CH₂ REGION (cont'd)

EU OU 121 122 123 124 125 126 127 128 129 130 131 132 133 134 135 136 137 138 139
 INDEX INDEX PM3 PM5 RABBIT PGAMMA RAB PAB P2A2 39-PA19 CT-12 PIKA HA-3 HA-11 HA-1 HA-5 HA-17 SYRIAN GEP SP
 'CL 'CL IGG 'CL IGG 'CL 'CL 20B 'CL HAMSTER TSP-13G

HEAVY CONSTANT CHAINS CH₂ REGION (cont'd)

HEAVY CONSTANT CHAINS CH2 REGION (cont'd)

EU INDEX	OU INDEX	156				157				158				159				# OF SEQUENCES	# OF AMINO ACIDS	OCCURRENCES OF MOST COMMON AMINO ACID	VARIABILITY	
		Xenopus	J32(I) 'CL	J34(II) 'CL	J36(I) 'CL	J38(IV) 'CL	J12(IV) 'CL															
243A																		4 (VAL)				
243B																		4 (PRO)				
243C																		4 (SER)				
243D																		5 (THR)				
243E																		5 (PRO)				
243F																		5 (PRO)				
243G	230																	5 (PRO)				
243H	231																	18 (VAL)				
243I	232																	8 (VAL)				
244	231																	11 (+)				
245	232																	37 (ALA)			10.	
245A																		45 (PRO)			6.6	
245B																		55 (THR)				
245C																		9 (PRO)				
246	233	233																9 (PRO)				
247	234	234																44 (GLU), 41 (GLU)			21., 22.	
248	235	235																48 (LEU)			24.	
249	236	236																36 (LEU)			35.	
250	237	237																43 (GLY)			16.	
251	238	238																44 (GLY)			26.	
251A																		54 (PRO)			10.	
251B																		12 (CYS)				
252	239	239																8 (HIS)				
253	240	240																60 (SER)			13.	
254	241	241																73 (VAL)			11.	
255	242	242																62 (PHE)			17.	
256	243	243																36 (ILE)			21.	
257	244	243																47 (PHE)			9.7	
258	245	244																64 (PRO)			12., 13.	
259	246	245																65 (PRO)			11.	
260	247	246																41 (LYS)			23.	
261	248	247																35 (PRO)			27., 30.	
262	249	248																46 (LYS)			21., 23.	
263	250	250																57 (ASP), 56 (ASP)			13., 14.	
264	251	249																29 (THR)			35.	
265	252	250																66 (LEU)			10.	
266	253	251																41 (MET)			26.	
267	254	252																53 (ILE)			19., 21.	
268	255	253																47 (SER)			21.	
269	256	254																38 (ARG)			29.	
270	257	255																57 (THR)			16.	
271	258	256																48 (PRO)			10.	
272	259	257																31 (GLU), 29 (GLU)			34., 37.	
273	260	258																59 (VAL)			10.	
274	261	259																65 (PRO)			14.	
275	262	260																98 (CYS)			1.	
276	263	261																49 (VAL)			14.	
277	264	262																59 (VAL)			8.2	
278	265	263																50 (VAL)			14.	
279	266	264																48 (ASP)			5.	
280	267	265																42 (VAL)			18.	
281	268	266																54 (SER)			16.	
282	269	267																20 (ASP)			38.	
283	270	268																21 (ASP)			28.	
284	271	271																47 (ASP)			16.	
285	272	272																51 (PRO)			14.	
286	273	269																34 (GLU), 32 (GLU)			27., 29.	
287	274	274																57 (VAL)			7.6	
288	275	275																36 (GLN), 34 (GLN)			14., 16.	
289	276	270																48 (PHE)			3.4	
290	277	271																30 (SER)			25.	
291	278	272																78 (TRP)			4.7	
292	279	273																52 (TRP)			27.	
293	274	274																37 (VAL)			13.	
294	275	275																10 (ASP)			11.	
295	280	276																21 (ASP)			2.1.	
296	281	277																33 (GLU), 32 (GLU)			28.	
297	278	278																57 (VAL)				
298	279	279																30 (HIS)			39.	
299	282	280																23 (THR)			13.	
300	283	281																42 (ALA)			15.	
301	284	282																12 (LYS)			5.0	
302	285	283																34 (TRP)			30.	
303	286	285																39 (ASP)			38.	
304	287	284																25 (ASP)			41.	
305	288	285																16 (VAL)			35.	
306	289	286																34 (VAL)			7.5	
307	290	286																90 (LEU)			24.	
308	291	288																41 (+)			24.	
309	292	289																52 (ILE)			17.	
310	293	290																15 (GLN), 14 (GLN)			78., 83.	
311	294	291																46 (HIS)			17.	
312	295	292																49 (GLN), 46 (GLN)			16., 17.	
313	296	293																53 (ASP), 51 (ASP)			20.	
314	315	314																90 (TRP)			5.3	
315	316	315																54 (LEU)			16.	
316	317	316																35 (SER)			30.	
317	318	317																63 (GLY)			14.	
318	319	318																51 (LIS)			21.	
319	320																					

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